Effect Modifications in Causal Inference

Causal Inference: What If 4.1 -4.3

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Review Causal Inference Notation

1. Individual causal effects:

$$Y^{a=1} \quad \neq \quad Y^{a=0}$$

2. Average Causal Effect:

$$\Pr\left[Y^{a=1} = 1\right] \neq \Pr\left[Y^{a=0} = 1\right]$$

Review Effect Measures

1. Measures of Null Causal Effect:

- Risk Difference:

$$\Pr\left[Y^{a=1}=1\right]-\Pr\left[Y^{a=0}=1\right]=0$$

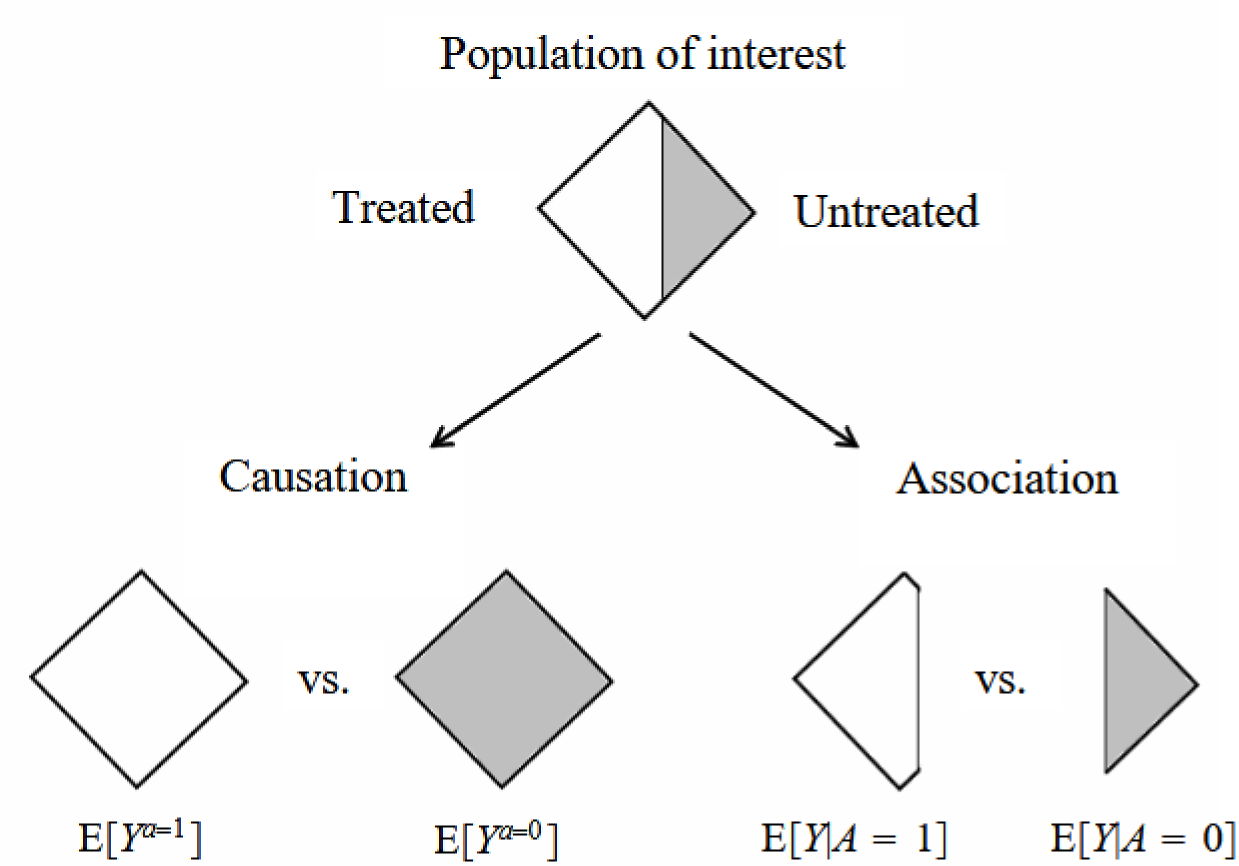
- Risk Ratio:

$$\frac{\Pr\left[Y^{a=1}=1\right]}{\Pr[Y^{a=0}=1]}=1$$

- Odds Ratio:

$$\frac{\Pr\left[Y^{a=1}=1\right]/\Pr\left[Y^{a=1}=0\right]}{\Pr[Y^{a=0}=1]/\Pr[Y^{a=0}=0]}=1$$

Review Causation V. Association



Review Randomization

1. Ideal/Marginalized Randomization ensures missing data (e.g. non-observed potential outcomes) occur by chance, this allows for exchangeability

2. Exchangeability:

$$Y^a \perp\!\!\!\perp A$$

3. Conditional Exchangeability:

$$Y^a \perp\!\!\!\perp A|L$$

Effect Modification Definition (4.1)

- *Modifier* V = Sex (1 female, 0 male)
- *Treatment* A = heart transplant (1 transplant, 0 no-transplant)
- *Outcome* Y = Mortality (1 death, 0 survival)
- Definition: V is a modifier of the effect of A on Y when the average causal effect of A on Y varies across levels of V

Effect Modification Example

Table 4.1

	V	Y^0	Y^1
Rheia	1	0	1
Demeter	1	0	0
Hestia	1	0	0
Hera	1	0	0
Artemis	1	1	1
Leto	1	0	1
Athena	1	1	1
Aphrodite	1	0	1
Persephone	1	1	1
Hebe	1	1	0
Kronos	0	1	0
Hades	0	0	0
Poseidon	0	1	0
Zeus	0	0	1
Apollo	0	1	0
Ares	0	1	1
Hephaestus	0	0	1
Cyclope	0	0	1
Hermes	0	1	0
Dionysus	0	1	0

Total Population

$\Pr[Y^{a=1} = 1] = 10/20 = 0.5$

$\Pr[Y^{a=0} = 1] = 10/20 = 0.5$

Risk Difference = 0

Risk Ratio = 1

Females V = 1

$\Pr[Y^{a=1} = 1]$ = 6/10

$\Pr[Y^{a=0} = 1]$ = 4/10

Risk Difference = 0.2

Risk Ratio = 1.5

Males V = 0

$\Pr[Y^{a=1} = 1]$ = 4/10

$\Pr[Y^{a=0} = 1]$ = 6/10

Risk Difference = -0.2

Risk Ratio = 2/3

- null average causal effect in the population does not imply a null average causal effect in a particular subset of the population
- generally we can expect some level of heterogeneity of individual causal effects because of variations in susceptibility

Additive, Multiplicative, and Qualitative Modification

- Sex V is an effect modifier of the treatment of heart transplant A on mortality Y on the **additive** scale because **risk difference** varies across levels of V.

- Sex V is an effect modifier of the treatment of heart transplant A on mortality Y on the **multiplicative** scale because the causal **risk ratio** varies across the levels of V.

- **Qualitative** effect modification occurs when the average causal effects in the subsets V are in the opposite direction.

How Causal Effect Depends on Effect Measured

- Since the average causal effect can be measured using different effect measures, the presence of effect depends of the effect measure being used.
- With **qualitative** effects, additive implies multiplicative and vice versa.
- With **non-qualitative** effects, you can find an effect on one scale and not the other.

Multiplicative, but not additive, effect modification by V:
$\Pr[Y^{a=0} = 1|V = 1] = 0.8$
$\Pr[Y^{a=1} = 1|V = 1] = 0.9$
$\Pr[Y^{a=0} = 1|V = 0] = 0.1$
$\Pr[Y^{a=1} = 1|V = 0] = 0.2$

Stratification to Identify Effect Modification Example

Greeks

Table 2.2

	L	A	Y
Rheia	0	0	0
Kronos	0	0	1
Demeter	0	0	0
Hades	0	0	0
Hestia	0	1	0
Poseidon	0	1	0
Hera	0	1	0
Zeus	0	1	1
Artemis	1	0	1
Apollo	1	0	1
Leto	1	0	0
Ares	1	1	1
Athena	1	1	1
Hephaestus	1	1	1
Aphrodite	1	1	1
Cyclope	1	1	1
Persephone	1	1	1
Hermes	1	1	0
Hebe	1	1	0
Dionysus	1	1	0

Romans

Table 4.2
Stratum $V = 0$

	L	A	Y
Cybele	0	0	0
Saturn	0	0	1
Ceres	0	0	0
Pluto	0	0	0
Vesta	0	1	0
Neptune	0	1	0
Juno	0	1	1
Jupiter	0	1	1
Diana	1	0	0
Phoebus	1	0	1
Latona	1	0	0
Mars	1	1	1
Minerva	1	1	1
Vulcan	1	1	1
Venus	1	1	1
Seneca	1	1	1
Proserpina	1	1	1
Mercury	1	1	0
Juventas	1	1	0
Bacchus	1	1	0

Given: Conditional exchangeability: $Y^a \perp\!\!\!\perp A|L$ for all a

$$\Pr[Y^{a=1} = 1|L = 1] / \Pr[Y^{a=0} = 1|L = 1]$$

$$\parallel$$

$$\Pr[Y = 1|L = 1, A = 1] / \Pr[Y = 1|L = 1, A = 0]$$

Greeks:	Romans
$\Pr[Y = 1\|L = 0, A = 1] = \frac{1}{4}$	=1/2
$\Pr[Y = 1\|L = 0, A = 0] = \frac{1}{4}$	=1/4
$\Pr[Y = 1\|L = 1, A = 1]$ = 2/3	=2/3
$\Pr[Y = 1\|L = 1, A = 0]$ = 2/3	=1/3
$\Pr[Y^{a=1} = 1]$ $\frac{1}{4} \times 0.4 + \frac{2}{3} \times 0.6 = 0.5$	½ x 0.4 + 2/3 x 0.6 = 0.6
$\Pr[Y^{a=0} = 1]$ ¼ x 0.4 + 2/3 x 0.6 = 0.5	¼ x 0.4 + 1/3 x 0.6 = 0.3
Causal Risk Difference = 0	Causal Risk Difference = 0.3
Causal Risk Ratio = 1	Causal Risk Ratio = 2

- Target trial = Measure effect of treatment of heart transplant A conditionally randomized based on severity L, with stratification between countries V, for outcome mortality Y.

Why to Care About Modifiers

- If V modifies the effect of treatment A on the outcome Y then the average causal effect will differ between populations with different prevalence of V.
- The presence of effect modification is helpful to identify the groups of individuals that would benefit the most from the intervention.
- Identifying effect modification may help understand the mechanism leading to the outcome.

Discussion Questions

1. Why isn't the odds ratio scale a desirable parameter of interest for causal inference?

2. Why is the additive (risk difference) over the multiplicative (risk ratio) preferred to identify groups that will benefit the most from the intervention?

3. How will matching across strata impact the assessment of effect modifiers (example Silber 2016) https://jamanetwork.com/journals/jamasurgery/fullarticle/2482670?appId=scweb